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OBITUARY NOTICE

OF

ARTHUR ROBERTSON CUSHNY.

(WITH PORTRAIT.)

1866–1926.

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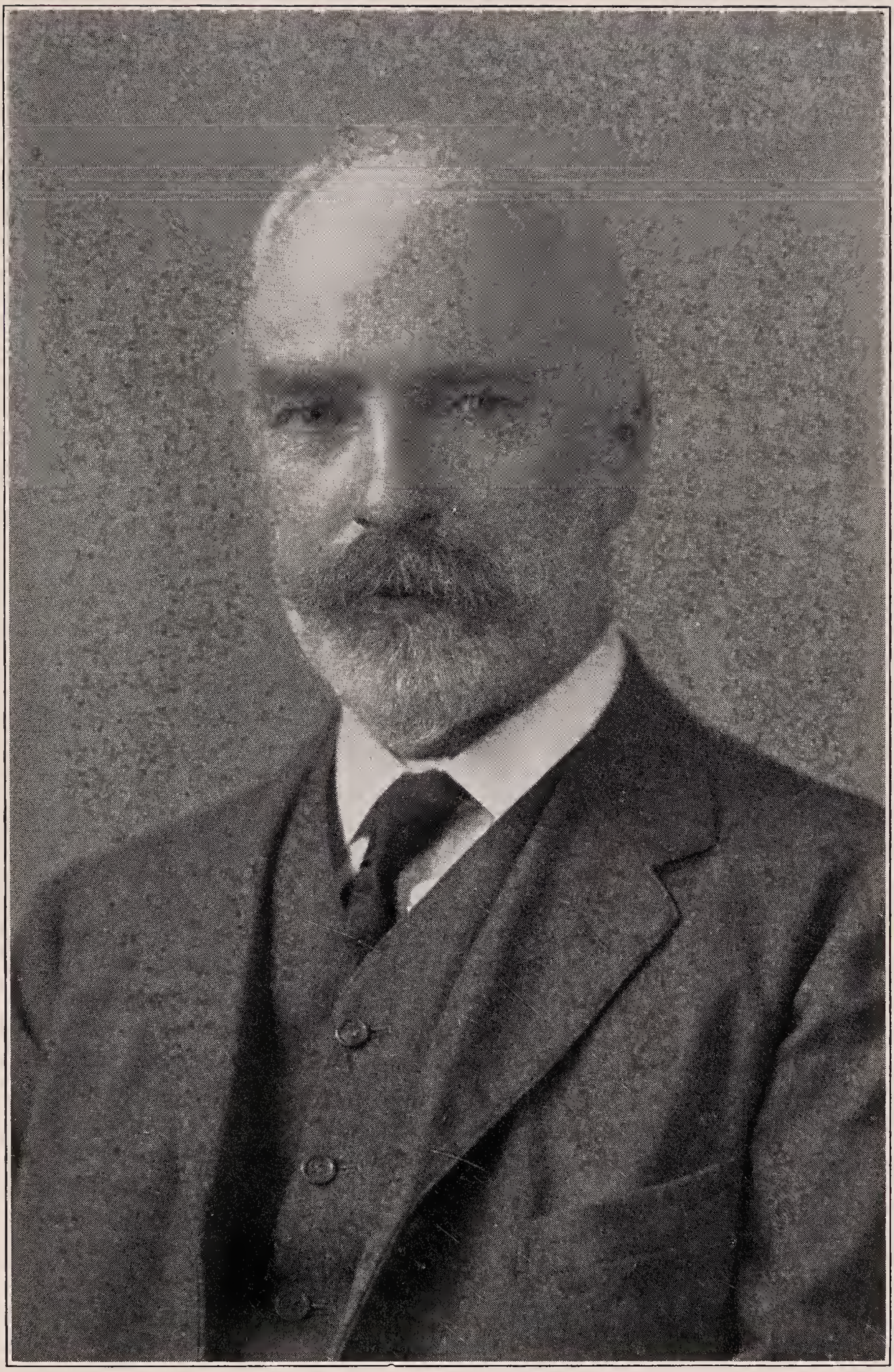

Arthur R. Cushny.

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ARTHUR ROBERTSON CUSHNY—1866–1926.

A. R. CUSHNY, who died suddenly on February 24th of this year, at the early age of 60 years, was by common consent the leading Pharmacologist of this country. The course of his career, moreover, had taken him into other countries, where he was known and honoured as in his own, so that his reputation and authority in his own subject, and in a wider field of experimental medicine, were truly international.

Cushny was the fourth son of a Scottish clergyman, and was born on March 6th, 1866, at Fochabers, in Morayshire. He passed from the local school to the University of Aberdeen, where he graduated M.A. in 1886. Before this graduation he had already chosen the profession of medicine, and had entered as a student at the Marischal College, from which in 1889 he graduated M.B., C.M., with the highest honours.

At that time there were but few centres in Britain in which Pharmacology was presented as a definite branch of experimental science by a teacher devoting his whole time and interest to the subject. Aberdeen, however, was of the few, and Cushny had the good fortune to come under the influence of John Theodore Cash, to whose teaching he attributed the awakening of his interest in Pharmacology, and his early decision to make it his life's work. Accordingly, when Cushny in the year of his medical graduation was awarded the George Thompson Fellowship by his University, and left Britain, at the age of 23, to study on the Continent, he had already a definite aim ; and the choice thus made, under the influence of Cash, was soon to be confirmed by an association lasting several years with Oswald Schmiedeberg. His first object, however, on leaving Aberdeen was to widen his experience of physiological technique. He spent a year in Berne, studying under Kronecker, and a short period in Würzburg, before settling in Strassburg, then the most famous centre of pharmacological teaching and research in Europe. Schmiedeberg, indeed, had done more than any other one man to promote the application, in German-speaking countries, of the newly developed methods of physiology and biochemistry to the study of the action of drugs and remedies, and thus to replace the traditional " materia medica " and empirical " therapeutics " of the old medical curriculum by the experimental science of Pharmacology ; and the new tradition, which he did so much to create, was carried to other countries largely by his pupils. With Schmiedeberg, therefore, Cushny was bound to find full opportunity for following his chosen course.

After a year's research work as a guest in the Institute, he accepted appointment as assistant to the Professor, and remained in this position during 1892 and 1893. As co-assistants, whom he always kept in affectionate remembrance, he had C. G. Santesson and E. P. Poulsson, professors of Pharmacology now in Stockholm and Oslo respectively, and Fr. Pfaff, formerly professor of Pharmacology at Harvard. Cushny's own publications direct from the Strassburg Institute included papers on anæsthesia with chloroform and ether, on the active principles of gelsemium, and on the action of muscarine on the frog's heart. He had also begun investigations on sparteine and on the poison of castor-oil seeds, which were finished and published after he had migrated elsewhere. For Schmiedeberg he formed, and always kept, a deep admiration and regard, which found public expression when, in due course, he dedicated his own great text-book "dem Meister vom Schüler." At the same time Cushny probably had, towards the end of his period in Strassburg, a conviction which he certainly held in later years, that the influence of Schmiedeberg and his school, like that of most reformers, had caused the pendulum to swing for the time too far. The new Pharmacology, with its sceptical aloofness from therapeutic effects which could not be analysed by laboratory methods, was tending to lose contact with practical medicine. That some feeling of this kind was growing in Cushny's mind, on the eve of the next important step in his career, is strongly suggested by the fact, recorded by Prof. J. J. Abel, that in 1893 Cushny had planned to return to Britain, and to seek opportunity for combining laboratory research with clinical work in a hospital and consulting practice. Abel himself had just vacated the chair of Pharmacology at the University of Ann Arbor, Michigan, on appointment to that at Johns Hopkins, and had been commissioned, on visiting Europe, to find a successor. Apparently he had some difficulty in persuading Cushny to accept a position which would afford no direct opportunities of contact with clinical work, and would cut him off definitely from medical practice. However that may be, Cushny accepted the invitation to Ann Arbor, and left Strassburg, at the age of 27 years, for the Chair which he was to hold with great and growing distinction for the next twelve years.

In the first few years at Ann Arbor, so far as the published record gives indication, the new professor would appear to have been engaged in completing investigations of somewhat minor importance, already begun at Strassburg. In addition to some already mentioned, there is a paper in 1896, in the first volume of the newly founded *Journal of Experimental Medicine*, on the toxicity of piperidine, coniine and intermediate bases. By this time, however, Cushny must have already begun his attack on one of the major problems of Pharmacology, which was to hold his interest for the remainder of his life, with results which, by themselves, would have given him high rank among workers in Pharmacology and Therapeutics. In the second volume of the *Journal of Experimental Medicine*, in 1897, he published a long and important paper on the action of substances of the digitalis series on the circulation in mammals. The pharmacological literature on the series was already enormous, but, as Cushny pointed out, the direct experimental observations of their action on the heart had almost all been made on cold-blooded animals, the demonstration of their action on the circulation in mammals having been practically confined to records of the arterial blood-pressure. The work of Roy and Adami on the use of the myocardiograph had appeared shortly before Cushny's migration to Ann Arbor, and the new method gave him the opportunity of directly recording the effects of digitalis and its allies on the muscular contractions of the different chambers of the mammalian heart. This paper, giving the results of Cushny's first completely independent investigation, in a field of his own choice, has rightly come to be regarded as a classical contribution to the subject with which it deals. As indicated above, it was the first of a series, published at wide intervals, dealing with one of his chief scientific interests. His mature views on the subject were presented in a monograph on "The Action and Uses in Medicine of Digitalis and its Allies," published as recently as 1925.

Having completed his masterly account of the action of digitalis on the normal mammalian heart and circulation, Cushny was evidently impressed with the lack of clear knowledge concerning the defects of the heart's action, responsible for the various forms of irregular pulse encountered in human patients. In the absence of such knowledge no rational transfer could be made of his pharmacological data to therapeutic practice. Those were days before the polygraph and the string galvanometer; conditions which, through the work of Mackenzie, Lewis and others have now been so thoroughly analysed, seemed then to present an inextricable tangle. Cushny, therefore, set himself the task of producing artificial irregularities in the mammalian heart by direct stimulation of its chambers, and of comparing the irregularities of pulse thus produced with those recorded by the sphygmograph in the clinic. A preliminary paper on some of the physiological results was already published with S. A. Matthews in 1897, but the full exposition of their significance, in the interpretation of pulse records, was not given till 1899 (*Journal of Experimental Medicine*, vol. 4). In this paper Cushny, by comparing the records of irregularities produced experimentally with those shown in pulse records obtained from patients, was able in the latter to distinguish premature contractions of the auricle from those originating in the ventricle. These premature contractions had simultaneously been identified by Wenckebach, who called them "extra-systoles," and similarly identified their points of origin, with the aid of Cushny and Matthews' published physiological records. The successful analysis of these recognisable types of intermittence occupies the main part of Cushny's paper, and shows him to have been well in advance of other workers at that time. It was really transcended in importance, however, by a suggestion which, with characteristic modesty and reserve, he put forward in a short paragraph supplementary to his main thesis. "A few words," he wrote, "may be added in regard to the extreme irregularity of the heart known clinically as delirium cordis . . . . The clinical sphygmogram in these cases resembles exactly that obtained from dogs when the auricle is undergoing fibrillary contractions, which may be continued for a long time without proving fatal. I do not wish to assert that the clinical delirium cordis is identical with the physiological delirium auriculæ, but the resemblance is certainly striking."

It were idle to speculate on the change which might have been produced in the history of cardiology during the ensuing ten years, if Cushny had felt sufficient confidence in its value to follow up this suggestion. Already he held the clue to the meaning of an important type of clinical irregularity, and that type was pre-eminently the one in which benefit was to be obtained by the action of drugs of the digitalis series, which had formed the starting-point of Cushny's whole investigation. Probably the clinical recognition of the condition was not yet sufficiently definite to make Cushny feel sure of his ground; for whatever reason, he did not pursue the investigation at the time. Some seven years later, in conjunction with C. W. Edmunds, he again drew attention to the practical identity of the pulse-record from a particular case of this persistent irregularity with that obtained from a dog, in which auricular fibrillation had been experimentally produced. At this later date clinical cardiology was showing a rapid advance, largely owing to the introduction and application of the polygraph by James Mackenzie. From evidence obtained with that instrument, Mackenzie attributed the condition of persistent irregularity to origin of the rhythm in the auriculo-ventricular node, having apparently considered the possibility of auricular fibrillation, but rejected it, through ignorance of Cushny's evidence, or failure to appreciate its significance.

It was not until 1909 that Lewis in this country, and Rothberger and Winterberg in Vienna, independently established, by the use of Einthoven's string galvanometer, the correctness of the suggestion originally made ten years earlier by Cushny. Mackenzie also was then quickly convinced that the condition which he had called "nodal rhythm" was the result of auricular fibrillation; and, since an important feature of his own work during the preceding years had been to demonstrate that the cases of "nodal rhythm" were those in which digitalis and its allies showed their most definite therapeutic action, this conclusion could now be transferred to the condition of auricular fibrillation, which Cushny had so many years earlier produced experimentally, and tentatively recognised in the clinic. There remained the problem of explaining this therapeutic effect, in terms of what was known of the mode of action of digitalis, and to this Cushny devoted much further investigation. He welcomed the opportunity of collaboration with Sir James Mackenzie in clinical observations, and returned to the question more than once in laboratory research, seeking always to define the parts played in the therapeutic result by the different aspects and phases of the action of digitalis on the normal heart, as he had clearly differentiated them in his earliest paper on the subject.

Cushny's work at Ann Arbor was by no means limited to these fundamental investigations on the pharmacology of digitalis and the therapeutics of heart disease. With G. B. Wallace he published investigations on the action of saline cathartics, he wrote with characteristic balance and sanity on the use of alcohol in therapeutics, and he had already entered on the two other main lines of investigation with which, together with those on digitalis, his name will probably be most clearly and permanently associated—that on the contrasted actions of optical isomers, and that on the mechanism of urinary secretion. Beyond all this, in 1899, the year of his great paper on cardiac irregularities, he completed and brought to publication his "Text-Book of Pharmacology and Therapeutics." The only real predecessor to this book, in the same field, was the "Grundriss der Arzneimittellehre" of Cushny's teacher, Schmiedeberg. Something in its general scheme, and in its approach to the subject from the experimental side, Cushny's book was bound to owe to this model. The debt, however, was only of this general kind, and it may safely be claimed for Cushny's great work that it was the first text-book of the subject in any language to consider and to meet the needs of student and scientific physician alike; for, while taking his stand firmly on the results of exact experiment, Cushny had always the practical end in view, in accordance with the book's sub-title—"The action of drugs in health and disease." The book rapidly established itself with teachers, students and practitioners in the English-speaking world, and has played a very important part in the great development of pharmacological teaching and research since its publication. Throughout the rest of his life Cushny worked steadily to improve his book and to embody in successive editions the latest results of sound investigation. By constant resifting of the older work, and replacement of what was obsolescent, either in the list of remedies or in the evidence concerning their action, by what was of fresh value or importance, he contrived that the book should retain its original scope and character through all changes of detail, and in spite of the enormous growth of the published evidence calling for consideration.

In 1905 University College, London, decided to found a full professorship in Pharmacology. Teaching in the subject had previously been given by one of the physicians on the staff of the associated hospital; and the arrangement had, indeed, given opportunity to one, at least, who was by instinct and achievement a great experimental pharmacologist, though practising as a physician—Sidney Ringer. The subject, however, was attaining such independent importance that a man was needed who would give his whole time to teaching it, and to promoting research in it by his influence and example. Cushny was induced to accept the new Chair, and held it for the ensuing thirteen years. In this case he did not, as at Ann Arbor, succeed to a department already well organised and housed; he had to begin at the beginning, with no immediate prospect of more than one ill-lit room for his own research. Though accommodation was poor, however, the calls on his time for teaching and administration were relatively few, and he was soon busy again with the relation between optical isomerism and pharmacological action, with a new investigation of the action of drugs on the uterus, and, a little later, with the chemotherapeutic properties of antimony. The events already mentioned brought him back again, in 1909, to the study of cardiac irregularities and digitalis, in conjunction with Mackenzie and other clinical colleagues. In the circle of his more immediate colleagues, in the neighbouring faculties at University College, he soon established himself on a footing of close scientific and personal fellowship. In spite of his quiet and unassertive manner, his influence quickly made itself felt in various directions, and in scientific societies and Government departments alike his opinion was sought on all kinds of matters touching on Pharmacology. Later when, through a generous gift of the late Mr. Carnegie, Cushny was able to build a new and well-equipped Institute alongside that of Starling, younger pharmacologists from other British schools came to him as assistants, and from other countries as guests. He published an important paper on the alkaloids of Senecio (rag-wort), which he identified as the cause of hepatic cirrhosis following fodder-poisoning in cattle, a short one on nutmeg-poisoning, and a series, with different collaborators, on the pharmacology of the respiratory centre.

In the years immediately preceding the war he had returned to his investigation of the mechanism of urinary secretion, and was gathering and sorting the material for the important monograph on that subject which was published, as one of the series edited by Starling, in 1917. As a critical review, clear, cautious and fair, it immediately gained wide appreciation. This monograph and his text-book show Cushny as a writer at his best. He had a keen eye for the heart of a problem, and a truly remarkable faculty for reducing a bewildering mass of conflicting evidence to a coherent, balanced and readable statement. His literary style was exactly suited to his purpose. He used language with economy and scholarly precision, avoiding rhetoric as he shunned any kind of personal display. The most he allowed himself was an occasional glint of quiet humour. A few sentences may be quoted from the letter to Starling, as general editor, printed by way of preface to the monograph. They give a hint of the immense and conscientious labour which Cushny gave to this task, and are so characteristic of his manner and his attitude, that one who knew and loved him can almost hear him speak with his quiet chuckle. "No other organ of the body," he writes, "has suffered so much from poor work as the kidney, and in no other region of physiology does so much base coin pass as legal tender. It was therefore necessary to sift thoroughly this mass of printed matter of over 6,000 pages, and I have read it carefully and, as far as might be, sympathetically, though I must confess that my patience has been sorely tried by some papers in which the depth bore no proportion to the length. . . . And as my criticism had to be brief, it may sometimes appear more severe than I had designed ;

anyone who may feel himself aggrieved by it may find some consolation in the pages in which your own earlier papers and my own are critically discussed, where he will find that they also do not pass through the ordeal unscathed."

The theory of kidney secretion which Cushny himself put forward, and modestly termed the "modern" theory, was for him merely a rational framework, enabling him to make an orderly presentation of the existing knowledge. Like Starling, he had started with the view that an application of newer physical knowledge would suffice to rehabilitate Ludwig's theory, of filtration in the glomeruli and reabsorption in the tubules, in place of the Bowman-Heidenhain theory of vital secretion. His examination of the possibility produced evidence which any later speculations must take into account; in particular, Cushny's distinction of "threshold" and "non-threshold" substances will remain as a solid contribution to the subject. In the end he found himself driven, by the evidence of his own observations, to credit the tubule cells with a selective action. Part of the reabsorption theory seems to be more firmly established as evidence accumulates, but the question as to whether the non-threshold substances are concentrated wholly by a selective failure of reabsorption, as Cushny held, or are to any extent newly secreted through the tubule cells, remains for final settlement. Cushny's monograph brought the evidence to a new focus, and for many years will continue to provide a basis for further investigation.

Another monograph, dealing with the third chief interest of his working life, has yet to appear. This embodies the Dohme lectures given in Baltimore in 1925 on "The Biological Relations of Optically Isomeric Substances." In a series of papers, of fundamental importance for any ultimate theory of the nature of pharmacological action, Cushny had shown that the tissues of the higher animals, in their response to the intense and precisely localised actions of certain alkaloids and bases—the hyoscyamines, the hyoscines, the adrenalines—exhibit a selective relation to optical isomers, recalling that which Pasteur had long ago demonstrated for the unicellular organisms. The forthcoming monograph will give new opportunity for appreciating the significance of the whole series of related phenomena, in the calm light of Cushny's critical wisdom.

The war meant for Cushny, as for most others, a diversion of activity into new and unexpected channels. He worked hard on committees, of the Royal Society among other organisations, and responded loyally to the call soon made on Pharmacology, hitherto among the least warlike of the sciences. Undoubtedly he felt the strain which bore upon all, and the breaking of sympathies and personal contacts which he had prized.

In 1918 Cushny was invited to the chair of Pharmacology in Edinburgh, in succession to Sir Thomas Fraser. Fraser had held a joint chair of Materia Medica and Clinical Medicine, and it was proposed that the new Professor, while devoting himself to Pharmacology, should work in close association with a Professor of Clinical Therapeutics, who would give his whole time to investigation in the hospital. The post was therefore one which offered, not only a wider teaching opportunity than that at University College, but the promise of that regular contact with practical therapeutics which Cushny had always desired. Something of a Scotsman's hunger for the air of his native land probably helped to weigh the balance, and he decided once more to migrate. He adapted himself with his usual quiet efficiency to the new conditions, and was soon a trusted and influential adviser in the affairs of the Medical School and the University. During those last eight years there was no definite relaxation of his quiet, steady work in the subject of his choice. His two other monographs were written, in addition to new editions of his text-book and a series of original papers. He served on two international conferences on the biological standardisation of drugs—a method which he, indeed, had initiated during his period at Ann Arbor. He took a prominent part in the arrangements for the International Physiological Congress in Edinburgh in 1923, and showed himself eager, with gracious hospitality, to promote the renewal of scientific friendships which the war had interrupted. In 1925 he again travelled to the United States, to give the Dohme lectures at Baltimore, to receive an honorary degree from his old University, and to revisit many old friends. Only a few who knew him closely would have noticed a gradual withdrawal from the risks of fatigue and excitement in one who had always shunned the appearance of exertion. These few knew that for some years, through the chance of a class-room observation of his blood-pressure, he had been aware of a danger threatening his life. When the end came it was sudden, as he would have wished, and free from the lingering disability which had been his only fear.

Nobody can make a careful study even of Cushny's published work without obtaining some impression of his personality. Such a student will realise him not only as a man of deep and exact knowledge, and of ripe experience, but as one in whom pride and modesty combined to make it impossible that he should press the claims to recognition of his own discoveries. Probably few among the many who had a general sense of his authority and eminence in his own subject have appreciated the full importance and originality of his contribution to the therapeutics of heart disease ; still fewer, probably, know that Cushny first predicted the importance of antimony as a specific agent in protozoal infections, and himself produced the first suggestive evidence of its value, leaving to others, who rapidly invaded the territory thus opened, the detailed exploration, with all that it has meant for the control of tropical diseases. He had, indeed, an almost exaggerated fear of anything like display or pretention ; one had to penetrate the veil of a natural reserve to appreciate fully the solid worth of his character. He did not give his intimacy easily, but responded with a true warmth of affection when his confidence was won. The generosity of his help, to younger workers in his own field, none knows better than the writer of this notice. At a time when he hardly knew me, on my publication of a paper dealing with work in a field which he had himself begun to explore, he sought me out, with spontaneous warmth of approval and encouragement. As I came to know him better, it became natural to me to submit my observations or ideas to the test of his opinion. As many others must have done, I always found him generous with his interest and his time ; cautious and critical, he kept his mind open to new ideas, and seasoned his comment with a kindly humour. In the presence of loquacity or exaggerated enthusiasm, however, he retired behind a screen of whimsical boredom. To know him was to trust him absolutely, and to understand what it was which gave him such weight and authority with his students, and with colleages at the council board.

Cushny received honorary degrees from his old University of Aberdeen, and from that of his first professorship at Ann Arbor. He was elected to the Fellowship of the Royal Society in 1906, and served on its Council from 1916–1918.

Early in his period at Ann Arbor, Cushny married Sarah Fairbank, a young English lady whom he had met in Strassburg. Their home life was one of serene happiness and of charming hospitality to his students and colleagues. During his tenure of the Chair at University College they lived, with their one daughter, in Hampstead ; later, on removal to Edinburgh, they were able to secure an historic manor house, not far from the city, with a large and beautiful garden —Peffermill House, at Craigmillar, the "Dumbiedykes" of the Heart of Midlothian. Cushny's pleasure in this house, and especially in his garden, grew with the years, and he had begun to look forward to a quiet time in the future, when he could withdraw from public activity, and commune with the fathers of therapeutic science, in his library and among his plants ; but the blow fell suddenly, and he passed from the fullness of his powers into the final sleep.

H. H. D.

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